REMARKS

Claims 18, 21, 23, 25-30 are pending in the application after entry of the present amendment. Claims 18, 21, and 23 have been amended. Claims 19, 20, 22 and 24 have been canceled. Claims 25-30 have been added.

Substance of Interview

Applicant thanks the Examiner for the telephonic interview of April 29, 2004. Pursuant to 37 CFR 1.133(b), a Statement of the Substance of Interview is included with this response.

Amendments to the Specification

Response to Amendment

The Examiner has requested resubmission of the amendments filed on 21 January 2003, Paper 25, because the amendments were not marked up to show the changes made. Applicant submits that a marked up version of the amendments was properly presented in the Response to Office Communication mailed on 13 January 2003. In order to present a complete response to the current action, Applicant has resubmitted the amendments and respectfully request that the amendments be so entered.

Sequence Listing

Applicant submits a Sequence Listing complying with 37 CFR §1.821- 1.825 in connection with this paper. This paper is accompanied by a floppy disk containing the sequences, SEQ ID NO: 1-16, in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825. . Applicant requests that the Sequence Listing be entered into the Specification in place of the previously submitted Sequence Listing.

The specification has also been amended to introduce sequence identifiers for sequence SEQ ID NO:7-16. These sequences were previously identified in the specification, on page 6, by their Genbank accession numbers, thus, this amendment does not introduce new matter. Introduction of the sequences and sequence identifiers was done in the interest of clarifying claim language.

Claim Rejections - 35 U.S.C. §112, Second Paragraph

Claims 18-24 stand rejected under 35 U.S.C. §112, second paragraph as failing to particularly point out and distinctly claim the subject matter of the invention. Claims 19, 20, 22 and 24 have been canceled. The rejection as it stands against amended claims 18, 21, and 23 is respectfully traversed. Additionally, the rejection as it may be relevant to new claims 25-30 is discussed below.

The claims have been amended to specify that the Kir3.0 polypeptides recited in the claims are selected from the group consisting of polypeptides having homology with Kir3.0 polypeptides encoded by specific nucleic acid sequences.

Amended claim 18 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel; combining the candidate agent with the Kir3.0 channel under conditions which permit inward K+ current; and determining the induced current, wherein a reduction in the induced current in the presence of the candidate agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel, wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7 (previously identified by Genbank accession number L25264), a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11 (previously identified by Genbank accession number U24660), a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 (previously identified by Genbank accession number U11860) and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16 (previously identified by Genbank accession number L47208). The sequences were identified by their Genbank accession numbers in the specification as filed on page 6, thus, this amendment does not introduce new matter.

New claim 28 depends from claim 18 and recites that the Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 75% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the

nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 or a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. Support for claim 28 is found on page 8 of the specification as filed.

Amended claim 21 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising providing a functional Kir3.0 channel formed by introducing into an expression host cell a nucleic acid encoding a first mammalian Kir3.0 polypeptide and a nucleic acid encoding a second mammalian Kir3.0 polypeptide under conditions that permit expression of the nucleic acid, wherein the first and second mammalian Kir3.0 polypeptides are different from each other, and wherein the mammalian Kir3.0 polypeptides assemble to form a functional Kir3.0 in the expression host cell; combining a candidate agent with a functional Kir3.0 channel under conditions that permit inward K+ current; and determining the induced current, wherein a decrease in the induced current in the presence of the agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel, wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. The sequences were identified by their Genbank accession numbers in the specification as filed on page 6 , thus, this amendment does not introduce new matter.

New claim 29 depends from claim 21 and recites that the Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 75% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 or a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. Support for claim 28 is found on page 8 of the specification as filed.

Amended claim 23 recites a screening assay for identifying materials which inhibit the activity of a Kir3.0 channel, comprising the steps of introducing nucleic acid encoding a Kir3.0 channel formed from at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides into an expression system and causing the expression system to express the nucleic acid encoding a Kir3.0 channel; contacting the Kir3.0 channel with one or more candidate channel-inhibiting materials; and selecting candidate material(s) which inhibit the activity relative to a control performed in their absence, wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic

acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. The sequences were identified by their Genbank accession numbers in the specification as filed on page 6 , thus, this amendment does not introduce new matter.

New claim 30 depends from claim 23 and recites that the Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 75% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 or a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. Support for claim 28 is found on page 8 of the specification as filed.

New claim 25 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel; combining the candidate agent with the Kir3.0 channel under conditions which permit inward K+ current; and determining the induced current, wherein a reduction in the induced current in the presence of the candidate agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides encoded by nucleic acids that hybridize under low stringency conditions with a complement of the nucleic acid of SEQ ID NO: 7, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:16. This claim recites the limitations present in canceled claim 20 and does not introduce new matter.

New claim 26 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising providing a functional Kir3.0 channel formed by introducing into an expression host cell a nucleic acid encoding a first mammalian Kir3.0 polypeptide and a nucleic acid encoding a second mammalian Kir3.0 polypeptide under conditions that permit expression of the nucleic acid, wherein the first and second mammalian Kir3.0 polypeptides are different from each other, and wherein the mammalian Kir3.0 polypeptides assemble to form a functional Kir3.0 in the expression host cell; combining a candidate agent with a functional Kir3.0 channel under conditions that permit inward K+ current; and determining the induced current, wherein a decrease in the induced current in the presence of the agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides encoded by nucleic acids that hybridize under low stringency conditions with a complement of the nucleic acid of

SEQ ID NO: 7, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:16. This claim recites the limitations present in canceled claim 22 and does not introduce new matter.

New claim 27 recites a screening assay for identifying materials which inhibit the activity of a Kir3.0 channel, comprising the steps of introducing nucleic acid encoding a Kir3.0 channel formed from at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides into an expression system and causing the expression system to express the nucleic acid encoding a Kir3.0 channel; contacting the Kir3.0 channel with one or more candidate channel-inhibiting materials; and selecting candidate material(s) which inhibit the activity relative to a control performed in their absence, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides encoded by nucleic acids that hybridize under low stringency conditions with a complement of the nucleic acid of SEQ ID NO: 7, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:16. This claim recites the limitations present in canceled claim 24 and does not introduce new matter.

Applicant maintains the position that the claims as previously presented were not indefinite for reasons of record. One of skill in the art would understand what was meant by a Kir3.1 polypeptide, a Kir3.2 polypeptide, a Kir3.3 polypeptide and a Kir3.4 polypeptide as well as what is meant by a Kir3.0 channel. In further support of this position, Applicant attaches a reference (Coetzee, et al., "Molecular Diversity of K+ Channels, Annals N.Y. Acad. Sci.: 233-285, 1999) which indicates that the scientific community has adopted the terminology used in the present application and that several additional member of the Kir3.0 family have been identified and classified as Kir3.1, Kir3.2, Kir3.3, and Kir3.4 polypeptides. However, in the interest of expediting prosecution, the Applicant has amended the claims to recite homology to Kir3.0 polypeptides encoded by specific nucleic acid sequences.

The scope of Applicant's invention is readily determined from the language of amended claims 18, 21, 23 and new claims 25-30. The claims have been amended to specify that the Kir3.0 polypeptides recited in the claims are selected from the group consisting of polypeptides having homology with Kir3.0 polypeptides encoded by specific nucleic acid sequences. One of skill in the art would readily ascertain the scope of claims in context of the recited homologies. Applicant respectfully asserts that amended claims 18, 21, 23 and new claims 25-30 are in compliance with 35 U.S.C. §112, second paragraph and request withdrawal of the rejection.

Claim Rejections - 35 U.S.C. §112, First Paragraph

Claims 18-24 stand rejected under 35 U.S.C. §112, first paragraph as not being described in the specification so as to convey that Applicant has possession of the claimed invention. In particular, the Examiner asserts that the function and structure of Kir3.0, Kir3.1, Kir3.2, Kir3.3, and Kir3.4 are not adequately described by Applicant. Claims 19, 20, 22 and 24 have been canceled. The rejection as it stands against amended claims 18, 21, and 23 is respectfully traversed. Additionally, the rejection as it may be relevant to new claims 25-30 is discussed below.

Applicant again asserts that the structure and function of Kir3.0 (*e.g.*, comprised of individual members Kir3.1, Kir3.2, Kir3.3, and Kir3.4) is adequately identified and described in the claims, as well as in the specification. However, in the interest of expediting prosecution, the Applicant has amended the claims to specify that the Kir3.0 polypeptides recited in the claims are selected from the group consisting of polypeptides having homology with Kir3.0 polypeptides encoded by specific nucleic acid sequences. A more detailed discussion of the claim amendments is provided above in the section entitled **Claim Rejections - 35 U.S.C. §112, Second Paragraph.**

Applicant, in the specification as filed, set forth specific examples of nucleic acids encoding the Kir3.1, Kir3.2, Kir3.3 and Kir3.4 polypeptides. These nucleic acids were identified by their Genbank accession numbers and are now referred to by the sequence identifiers SEQ ID NOs: 7-16. The amendment of the claims to recite homology to the polypeptides produced from the recited nucleic acid sequences provides a structural definition of Kir3.0 polypeptides.

In addition, the unique properties of the functional multimeric Kir3.0 channels are demonstrated (page 27, lines 7-9; 24-25) in *Xenopus laevis* oocytes which are injected with atrial mRNAs (and mRNAs encoding serotonin receptor) wherein multimeric Kir3.0 channels are formed and inward rectifiers are opened by serotonin that is mediated by G-protein (*e.g.*, $G\beta_1\gamma_2$) activation. These multimeric Kir3.0 channels are further expressly demonstrated to exhibit the unique properties of conducting inward but not outward K^+ current, of exhibiting blockage by low concentrations of Ba^{2+}, and of exhibiting channel conductance that is dependent on voltage as well as $(E-E_K)$ (page 27, lines 8-12).

The specification further demonstrates that coexpression of Kir3.2/Kir3.1 in *Xenopus laevis* oocytes produces large G-protein mediated inward currents relative to the individual expression of either Kir3.2 or Kir3.1 (page 31, lines 2-9). The specification additionally describes that coexpression of Kir3.3/Kir3.1 in *Xenopus laevis* oocytes produces large inward currents relative to the expression of Kir3.3 alone (page 33, lines 14-24). Moreover, coexpression of Kir3.3 and Kir3.2 in *Xenopus laevis* oocytes produces small inward currents relative to the expression of Kir3.2 alone (page 33, lines 25-28).

For the foregoing reasons, the function and structure of the functional Kir3.0 (*e.g.*, Kir3.1, Kir3.2, Kir3.3, Kir3.4) heteromultimeric channels recited in Applicant's claims are more than sufficiently described in the specification in such a way as to reasonably convey to one skilled in the art that the Applicant had possession of the claimed invention at the time the application was filed. Applicant respectfully asserts that amended claims 18, 21, 23 and new claims 25-30 are in compliance with 35 U.S.C. §112, first paragraph and request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 102(b) - *Yatani, et al.* with evidence from *Krapivinsky, et al.*

Claims 18-20 stand rejected are rejected under 35 U.S.C. § 102(b) as being anticipated by *Yatani* with evidence from *Krapivinsky*. Claims 19 and 20 have been canceled. The rejection as it stands against amended claims 18 is respectfully traversed.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, "[t]o serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is **necessarily present** in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (emphasis added).

Amended claim 18 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel; combining the candidate agent with the Kir3.0 channel under conditions which permit inward K+ current; and determining the induced current, wherein a reduction in the induced current in the presence of the candidate agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel, wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4

polypeptide encoded by the nucleic acid of SEQ ID NO:16. Thus, amended claim 18 requires homology to Kir3.0 polypeptides encoded by the recited nucleic acid sequences.

The Examiner characterizes *Yatani* as teaching the method of reducing the current of a Kir3.0 channel with NAD and PTX. The Examiner further states that the "isolated cells of *Yatani* continuously synthesizes and combines the heteromeric subunits to form the inward rectifer channels meeting the amended claim limitation." The Examiner relies on *Krapinvinsky* to teach that the *Yatani* potassium channels are inherently heteromultimers.

Applicant respectfully asserts that *Yatani* does not teach the invention as defined in amended claim 18. The analysis of the potassium channels of *Yatani* is performed using inside-out patches of membranes; thus *Yatani* does not disclose cells that continually synthesize and combine heteromeric subunits to form the Kir3.0 channels. Furthermore, *Yatani* does not identify the composition of the channels studied. There is no sequence information disclosed. As such, *Yatani* cannot anticipate claim 18 which now recites homology to Kir3.0 encoded by specific nucleic acid sequences.

Krapivinsky cannot be used supplement *Yatani* in such a way as to show that *Yatani* anticipates claim 18. *Krapivinsky* was cited by the Examiner as showing that the channels of *Yatani* are heteromultimers. However, *Krapivinsky* does not show that that the channels of *Yatani* necessarily are composed of Kir3.0 polypeptides that are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. Applicant respectfully requests that the 35 U.S.C. § 102(b) rejection of amended claim 18 over *Yatani, et al.* with evidence from *Krapivinsky, et al.* be withdrawn.

Rejection Under 35 U.S.C. § 102(b) - *Karschin et al.* with evidence from *Krapivinsky et al.*

Claims 18-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by *Karschin* with evidence from *Krapivinsky*. Claims 19 and 20 have been canceled. The rejection as it stands against amended claims 18 is respectfully traversed.

As stated above, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal*

Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, "[t]o serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

Amended claim 18 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel; combining the candidate agent with the Kir3.0 channel under conditions which permit inward K+ current; and determining the induced current, wherein a reduction in the induced current in the presence of the candidate agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel, wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. Thus, amended claim 18 requires homology to Kir3.0 polypeptides encoded by the recited nucleic acid sequences.

The Examiner characterizes *Karschin* as disclosing the 5-HT/5-HT receptor and Ach/Ach receptor activations of I(Kach) inwardly rectifying potassium current. The Examiner further states that the isolated cells of *Karschin* continuously synthesizes and combine the heteromeric subunits to form the inward rectifer channels meeting the amended claim limitation. The Examiner relies on *Krapinvinsky* to teach that the *Karschin* potassium channels are inherently heteromultimers.

The Applicant respectfully asserts that *Karschin* does not teach the invention as defined in amended claim 18. As stated in previous responses, *Karschin* only discloses heterologously expressed serotonin receptors which are activated by serotonin and acetylcholine in rat atrial (cardiac) myocytes containing endogenous K^+ channels. Although *Karschin* may disclose that recombinantly expressed serotonin receptors couple to native K^+ channels (*e.g.*, via a G-protein interaction) that are endogenous to rat atrial myocytes, nothing in the reference teaches or discloses combining at least two different inward rectifier, G-protein activated mammalian, potassium Kir3.0

polypeptides to form functional Kir3.0 channels, where the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

As with the *Yatani* reference, *Krapivinsky* cannot be used to supplement *Karschin* in such a way as to show that *Karschin* anticipates claim 18. *Krapivinsky* was cited by the Examiner as showing that the channels of *Karschin* are heteromultimers. However, *Krapivinsky* does not show that that the channels of *Karschin* necessarily are composed of Kir3.0 polypeptides that are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. Applicant respectfully requests that the 35 U.S.C. § 102(b) rejection of amended claim 18 over *Karschin* with evidence from *Krapivinsky* be withdrawn.

Rejection Under 35 U.S.C. § 102(a) - Duprat, *et al.*

Claims 18-24 stand rejected are rejected under 35 U.S.C. § 102(b) as being anticipated by *Karschin* with evidence from *Krapivinsky*. Claims 19, 20, 22, and 24 have been canceled. The rejection as it stands against amended claims 18, 21 and 23 is respectfully traversed.

Amended claim 18 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel; combining the candidate agent with the Kir3.0 channel under conditions which permit inward K+ current; and determining the induced current, wherein a reduction in the induced current in the presence of the candidate agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel, wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

Amended claim 21 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising providing a functional Kir3.0 channel formed by introducing into an expression host cell a nucleic acid encoding a first mammalian Kir3.0 polypeptide and a nucleic acid encoding a second mammalian Kir3.0 polypeptide under conditions that permit expression of the nucleic acid, wherein the first and second mammalian Kir3.0 polypeptides are different from each other, and wherein the mammalian Kir3.0 polypeptides assemble to form a functional Kir3.0 in the expression host cell; combining a candidate agent with a functional Kir3.0 channel under conditions that permit inward K+ current; and determining the induced current, wherein a decrease in the induced current in the presence of the agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

Amended claim 23 recites a screening assay for identifying materials which inhibit the activity of a Kir3.0 channel, comprising the steps of introducing nucleic acid encoding a Kir3.0 channel formed from at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides into an expression system and causing the expression system to express the nucleic acid encoding a Kir3.0 channel; contacting the Kir3.0 channel with one or more candidate channel-inhibiting materials; and selecting candidate material(s) which inhibit the activity relative to a control performed in their absence, wherein the Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

Thus, amended claims 18, 21 and 23 refer to homologous Kir3.0 polypeptides encoded by the recited nucleic acid sequences.

The Examiner characterizes *Duprat et al.* as teaching the inhibition of inward rectifier currents in various K^+ channels due to the presence of ATP and/or Mg^{2+}. However, *Duprat* does not teach Kir3.0 channels composed of Kir3.0 polypeptides are selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1

polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16. As such *Duprat* cannot anticipate the claims as amended.

Applicant respectfully requests that the 35 U.S.C. § 102(a) rejection of amended claims 18, 21, and 23 over *Duprat* be withdrawn.

Nonstatutory Double Patenting

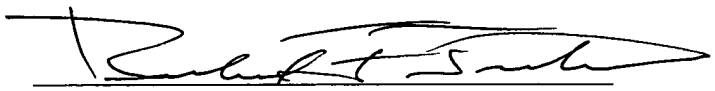
Claims 18-24 stand rejected under the judicially created doctrine of obviousness-type double-patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,734,021 in view of *Duprat* and *Yatani* evidenced by *Krapivinsky*.

Claims 1-5 of U.S. Patent No. 5,734,021 do not teach or suggest Kir3.0 channels channels composed of Kir3.0 polypeptides selected from the group consisting of Kir3.0 polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16 as set forth in the amended claims. Furthermore, for the reasons discussed above in regard to the 35 U.S.C.§102 rejections, *Duprat* and *Yatani* as evidenced by *Krapivinsky* do not fairly teach or suggest the invention as now defined in the pending claims. As such, Applicant respectfully requests withdrawal of the double-patenting rejection.

Applicant submits that the claims are in form for allowance and early notice of such is requested. If the Examiner believes that there are remaining issues which may be resolved by telephone, he is invited to call the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP



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